UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE VALSARTAN, LOSARTAN, AND IRBESARTAN PRODUCTS LIABILITY LITIGATION	**MDL No. 2875**
THIS DOCUMENT RELATES TO ALL CASES	**HON. ROBERT B. KUGLER** **CIVIL NO. 19-2875 (RBK)**

PLAINTIFFS' BRIEF IN OPPOSITION TO DEFENDANTS' MOTION TO EXCLUDE OPINIONS OF RON NAJAFI, PH.D.

HOLLIS LAW FIRM
8101 College Blvd, Suite 260
Overland Park, KS 66210
913-385-5400
913-385-5402 fax
Brett@HollisLawFirm.com

On the Brief:
C. Brett Vaughn RN, BSN, JD

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Cases

Rules

PRELIMINARY STATEMENT

Dr. Ronald Najafi, a Ph.D. organic chemist, submitted a terse, seven-page declaration in support of Plaintiffs' class certification motion, and it is only his class certification opinions that are at issue at this stage. Defendants purposely ignore the context and purpose of Dr. Najafi's *class certification* declaration. The opinion at issue addressed the relatively unremarkable proposition that NDMA and NDEA contamination is common to all class members. As is apparent by the seven-page declaration and Dr. Najafi's deposition testimony, the opinion was provided in support of class certification only and was not intended to be his full merits analysis and opinions. In fact, as Defendants are aware, Plaintiffs have not served all of their merits liability expert reports on organic chemistry and related issues.

Underlying this class certification opinion is the fundamental proposition that the genotoxic, carcinogenic impurities—NDMA and NDEA—should never have been in VCDs, and that VCDs with NDMA or NDEA present are not the same as or chemically equivalent to the approved formulations and impurity profiles of the Reference Listed Drugs, branded Diovan and Exforge. Dr. Najafi reaches his conclusion by applying regulatory and industry guidance, and his decades of education and experience, and Defendants' own records and regulatory findings that confirm the presence of nitrosamines in Defendants' valsartan products (which is why they were recalled and the FDA found them to be adulterated). Dr. Najafi's methodology is reliable, and his conclusions certainly are relevant and helpful. More importantly, at this class certification stage, whether Dr, Najafi is right or wrong is immaterial; his opinions demonstrate a question (e.g., "sameness" or chemical equivalency) common to all class members.

Defendants' lengthy motion is more notable for what it does not challenge than what it does. Defendants do not challenge Dr. Najafi's qualifications as a chemist. They do not dispute that his

opinions commonly apply to all class members. They do not even challenge some of Dr. Najafi's foundational opinions, such as "NDMA and NDEA (nitrosamines) are not new, nor unexpected impurities" and that "[t]he manner in which nitrosamines are formed is a **matter of basic chemistry**." (ECF 2033-3, Najafi Expert Decl. at ¶ 25, 26 (emphasis added)).

Rather, Defendants raise four main arguments, none of which warrant the exclusion of Dr. Najafi's opinions at this class stage.

First, Defendants question whether their valsartan needed to be the same or chemically equivalent to the branded products at all. Dr. Najafi reliably opines that Defendants' valsartan did not have the same "identity, strength, quality, and purity" of the branded equivalents (*See* Najafi Expert Decl. at ¶ 31-33), nor could they, given the undisputed nitrosamine contamination. This is the exact standard set forth by regulation, and as interpreted by the courts. Aside from this addressing the merits rather than class certification, and that the proposition flies in the face of the reality that their valsartan was recalled due to lack of equivalence, the foundation of this argument is false. Defendants are incorrect in their apparent assumption that their generic drugs can contain an infinite level of a dangerous, undisclosed carcinogen, thus have a materially different impurity profile, and still be considered the "same" as the branded drug. Again, this is a merits-based liability argument not at issue at this class stage. Dr. Najafi's methodology on this basic issue is reliable.

Second, certain Defendants' belief that not *all* of their recalled valsartan contained nitrosamines is an issue of weight, not admissibility. This includes Defendants' circuitous discussion about bioequivalence (which is irrelevant because it is a distinct requirement from sameness, chemical equivalence, or therapeutic equivalence), or purported variations in nitrosamine levels. Further, whatever the facts ultimately show is for the factfinder to decide after any class certification decision. Indeed, Defendants concede this. (*See* Def. Br. at 18) (whether Defendants

had obligation to make valsartan not containing nitrosamines "will, presumably, be addressed only if this Court certifies one o[r] more of Plaintiffs' putative classes.").

Third, Defendants simply repackage their April 13 motion to compel production of Dr. Najafi's testing and related records (ECF 2013-1) as a *Daubert* attack. Those attacks are irrelevant to the admissibility of his class certification opinions. Dr. Najafi properly relies on regulatory and industry sources for the proposition that Diovan and Exforge do not and should not contain nitrosamines (something some of Defendants' own experts admit). If Defendants wish to argue a contrary proposition to the factfinder later, the Court will determine whether that alternative universe argument will be permitted. But that does not affect the admissibility of Dr. Najafi's opinions now for purposes of demonstrating the predominance of common questions for all class members.

Finally, Defendants' afterthought argument that Dr. Najafi is "not qualified" to opine that "NDMA and NDEA are carcinogenic and should not be present" in Defendants' valsartan, because he is not a medical doctor or toxicologist, lacks merit. As the Court is well aware, Defendants' motion to exclude is set against the backdrop of a well-established scientific and regulatory consensus that NDMA and NDEA are part of what is called the *cohort of concern*—a small group of high potency genotoxic carcinogens where a compound-specific risk assessment is required. (Najafi Expert Decl. at ¶ 27-29). Dr. Najafi may rely on those regulatory determinations, which have been adopted by the FDA, in rendering his opinions, just as he relies on them in the scope of his ordinary-course duties as a chemist. Also, ironically, the upshot of Defendants' repackaged motion to compel argument appears to be that the testing methods and data generated by Dr. Najafi and his laboratory *are* reliable and he *can* reach conclusions about the presence of carcinogenic nitrosamines in drugs or not. Defendants cannot have it both ways.

For these reasons, discussed more fully below, Defendants' motion should be denied in its entirety.

APPLICABLE LAW

"Under the Federal Rules of Evidence, a trial judge acts as a 'gatekeeper' to ensure that 'any and all expert testimony or evidence is not only relevant, but also reliable.'" *Pineda v. Ford Motor Co.,* 520 F.3d 237, 243 (3d Cir. 2008) (citation omitted). Consistent with the "liberal thrust" of the federal rules of evidence, "Rule 702, which governs the admissibility of expert testimony, has a liberal policy of admissibility." *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 739 (3d Cir. 1994) (first quotation); *Pineda v. Ford Motor Co.*, 520 F.3d 237, 243 (3d Cir. 2008) (citation and quotation marks omitted) (second quotation). "Rule 702 has three major requirements: (1) the proffered witness must be an expert, i.e., must be qualified; (2) the expert must testify about matters requiring scientific, technical or specialized knowledge; and (3) the expert's testimony must assist the trier of fact." *Pineda v. Ford Motor Co.,* 520 F.3d 237, 244 (3d Cir. 2008).

ARGUMENT

I. Defendants Fail to Challenge Dr. Najafi's Class Certification Opinions

Notably, in this Circuit, "courts limit the *Daubert* inquiry to expert testimony offered to prove satisfaction of Rule 23's requirements." *In re Blood Reagents Antitrust Litig.*, 783 F.3d 183, 188 n.8 (3d Cir. 2015). Stated another way, the inquiry is limited to whether the expert's methods are reliable and useful to the questions to be addressed at class certification. *In re Processed Egg Products Antitrust Litig.*, 81 F. Supp 3d 412 (E.D. Penn, 2015). Defendants present no challenge to the thrust of Dr. Najafi's Declaration in support of class certification, which was "the presence of the nitrosamine contamination found in the Valsartan products at issue here renders these products as not the same as the Reference Listed Drug, Diovan and/or Exforge." (Najafi Expert Decl. at ¶ 3). Since this opinion is rooted in a reliable methodology, and is not truly challenged,

the motion should be denied in its entirety. As discussed below, the foundation for the class opinions is provided in the declaration, but that declaration was not intended as a full liability report as that phase has not yet been reached. At a later date, during the liability expert phase, Defendants can seek to challenge Dr. Najafi's merits opinions.

II. Dr. Najafi's Opinion That VCDs Containing NDMA or NDEA Are Not the Same or Chemically Equivalent to Novartis's RLDs Is a Reliable and Relevant Opinion

Defendants characterize Dr. Najafi's opinion that Defendants' generic Valsartan Containing Drugs ("VCDs") are not the same as the Reference Listed Drugs ("RLDs') as a "novel theory." This is a perplexing characterization, considering the mass recalls that have taken place worldwide of Defendants' generic VCDs due to the presence of mutagenic nitrosamines. (Def. Br. at 1). In essence, the Defendants seek to construct a context for their motion that ignores what has occurred in reality, facts that cannot be reasonably disputed.

A. The Impact NDMA or NDEA has on Bioequivalence is Irrelevant

Defendants claim that because Dr. Najafi acknowledged that a drug can contain harmful impurities and remain bioequivalent that he made an "admission [that] is fatal to his theory that the presence of NDMA or NDEA […] affected the sameness of Defendants' VCDs." (Def. Br. at 10). Ignored by Defendants is that bioequivalence in the sense that the VCDs still were capable of controlling blood pressure, is not at issue at all. Defendants' argument ignores that a generic drug must have identical strength, **quality, purity**, and potency as the RLD. (Najafi Expert Declaration at ¶ 18 (emphasis added)). This is hardly novel, but rather a basic fact that cannot be disputed. See 21 CFR 314.3(b). Genotoxic and mutagenic impurities that were never approved to be in the drug most definitely impact the quality and purity. Defendants' arguments are not even aligned with the opinions of their own expert Dr. Robbins, who opined that separate and apart from being bioequivalent, a generic drug must have "the **same safety profile** as the RLD." (Robbins Expert

Rpt. at ¶ 25, Ex. A). The presence of NDMA or NDEA in VCDs changes the safety profile of the drug from the RLD, therefore it is irrelevant whether the VCDs are still bioequivalent.

B. The Presence of NDMA or NDEA Impacts Both the Quality and Purity of Defendants' VCDs, Rendering Them Not the Same as the RLDs

The centerpiece of Defendants' motion is that "chemical equivalence" is not a phrase defined or recognized in the federal regulations. In the next breath, Defendants say that if "chemical equivalence" does happen to be defined in the law, then Dr. Najafi's opinion should still be excluded because it would then constitute an improper legal opinion. (Def. Br. at 1, 11). Defendants are wrong on both counts.

As an initial matter, Defendants' vacillating position would prevent any expert from being able to give the opinion that Defendants' VCDs are not the same as the RLDs or had a different chemical composition from the branded products. Chemical composition is a fact question, not an ultimate legal conclusion. Dr. Najafi is rightly able to opine on the *facts* of the chemical composition of Defendants' valsartan, and his conclusion is they are not generic equivalents, the same as, or chemically equivalent to, the RLDs. (Najafi Expert Decl. at ¶ 32 and 33).

Next, Defendants are incorrect that Dr. Najafi made-up a "chemical equivalence" standard or the duty of "sameness." Not so. Contrary to Defendants assertion, Dr. Najafi cites to 21 U.S.C 355(j) and 21 C.F.R. § 314.3(b) in paragraph 18 of his expert declaration, which reads:

> Generic drug manufacturers have an ongoing federal duty of sameness in their products. The generic manufacturer must demonstrate that their active ingredient(s) are the same as the Reference Listed Drug("RLD") and ***have identical strength, quality, purity, potency (and where applicable, other characteristics) as the RLD***.

(Najafi Expert Decl. at ¶18 (emphasis added)). He further confirmed this at his deposition:

[redacted]

*****

[redacted]

*****

[redacted]

*****

(ECF 2033-4, Najafi Dep. Tr. at 26:18-25, 27:7-28:11, 30:20-33:6, 34:19-22 (emphasis added).

Dr. Najafi's understanding is in accord with this Court's own discussion of the issue: "A marketed generic containing a contaminant cannot be the equivalent to the chemical entity listed in the Orange Book." (ECF 775, MTD Opinion 3 at 14). "All they had to know was they were buying a generic drug that contained valsartan because the very name "valsartan" or "valsartan-containing" constituted itself an express warranty that what plaintiffs were purchasing was the chemical equivalent of the Orange Book pharmaceutical." (MTD Opinion 3 at 14). Also, other federal jurisprudence and the FDA's interpretation of its own regulations. For instance, the Supreme Court has noted that a generic drug must be "chemically equivalent" to the branded drug. *See Mut. Pham. Co. Inc. v. Bartlett*, 570 U.S. 472, 477 (2013). The FDA has interpreted "same as" to mean "clinical

equivalence to the pioneer, chemical identity to the extent possible[.]" *Serono Labs., Inc. v. Shalala*, 158 F.3d 1313, 1321-22 (D.C. Cir. 1998). Court after court (including in cases involving some of Defendants here) has similarly recognized a "duty of sameness," and recognized "chemical equivalence" to be shorthand for the regulatory obligation that a generic drug "have identical strength, quality, purity, potency…as the RLD." *See, e.g.*, *Fulgenzi v. PLIVA, Inc.*, 711 F.3d 578, 581 (6th Cir. 2013) (An ANDA need only show ***that the generic drug is chemically and practically the same*** as its branded equivalent.") (emphasis added); *In re Zantac (Rantidine) Prods. Liab. Litig.*, 548 F. Supp. 3d 1225, 1248 (S.D. Fla. 2021) ("A generic drug manufacturer's duty under federal law is a duty of sameness, meaning that the manufacturer must ensure that its generic drug is the same as the brand-name equivalent drug in key respects. Thus, ***a generic drug's chemical composition and labeling must be the same*** as the brand-name equivalent drug.) (emphasis added) (intervening citations omitted); *Allergan Sales, LLC v. Teva Pharms. USA, Inc.*, No. 15-cv-01471, 2017 WL 3446634, at *2 (E.D. Tex. July 25, 2017) ("The generic drug must be ***chemically***, therapeutically, and biologically ***equivalent*** to the brand counterpart[.]") (emphasis added); *Elmazouni v. Mylan, Inc.*, 220 F. Supp. 3d 736, 742 (N.D. Tex. 2016) ("Federal law requires a generic drug to have the ***same chemical composition*** and labeling as its brand-name counterpart") (emphasis added); *Tsavaris v. Pfizer, Inc.*, 154 F. Supp. 3d 1327, 1334 (S.D. Fla. 2016) ("as a matter of federal law, ***a generic drug must be the chemical equivalent*** and bioequivalent of the brand name drug") (emphasis added); *Mylan, Inc. v. Comm'r of Internal Revenue*, 156 T.C. 17 (U.S. Tax. Ct. 2021) (generic manufacturer must demonstrate that the manufacturing process would preserve the generic drug's identity, strength, and purity"); *see also Sanofi-Aventis U.S. LLC v. FDA*, 842 F. Supp. 2d 195, 203 (D.C. 2012) (FDA may require information from generic applicant not only to compare impurity profile between generic and brand, but to request additional information "to

assess whether any difference in impurities would increase the likelihood of adverse consequences and thus be harmful to consumers").

Defendants' formulaic, semantic resistance to the existence of this requirement (i.e., "have identical strength, quality, purity, potency . . . as the RLD," *see* 21 U.S.C. § 355(j); 21 C.F.R. § 314.3(b)) is likely driven by their inability to credibly assert that the presence of unsafe levels of genotoxic carcinogens in their VCDs did not alter the quality or purity of the drugs, or the therapeutic equivalence of the drugs.[1]

Dr. Najafi lays out the interplay of various regulatory documents and how they relate to his class certification opinion, such as ICH M7(R1) identifying nitrosamines as part of a group of high potency mutagenic carcinogens referred to as the *cohort of concern* that must be independently assessed for permitted levels as occurred here, and due to the presence of NDMA and NDEA in Defendants' VCDs they are no longer the same as the RLDs per 21 U.S.C. § 355(j) and 21 C.F.R. § 314.3(b). (Najafi Expert Decl.). Courts in this Circuit (and elsewhere) routinely hold that expert testimony summarizing the complex regulatory regime governing drug approval and manufacture is appropriate and helpful. *See, e.g.*, *In re Suboxone Antitrust Litig.*, MDL No. 2445, No. 16-5073, 2020 WL 6887885 (E.D. Pa. Nov. 20, 2020) ("Numerous courts have found that 'the testimony of regulatory experts on the reasonableness of a pharmaceutical company's conduct in light of the complex nature of the FDA framework is helpful to a jury."). And of course this regulatory framework structures an appropriate methodology.

[1] Therapeutic equivalence refers to a generic drug's possessing the "same clinical effect and ***safety profile***." (FDA Orange Book, ECF 2036-7 at 8). VCDs that contain nitrosamines are not the same as, or chemical equivalent, or generic equivalent, or therapeutical equivalent of the RLDs on account of the nitrosamines' differing quality, impurity, and safety profile.

C. The RLDs Did Not Contain Nitrosamines

Defendants' fallback position is that, even if Dr. Najafi follows an appropriate standard (and as set forth above, he does), Dr. Najafi wrongly *assumes* a lack of chemical equivalence between Defendants' VCDs and the RLDs because, they argue, "Dr. Najafi *assumes* that the RLDs did not contain nitrosamines." (Def. Br. at 2 (emphasis added)). However, buried within their brief, Defendants actually acknowledge that Dr. Najafi relied on testing performed by the regulatory agency Health Canada in support of his so-called "assumption." (Def. Br. at 13). Health Canada testing revealed that the branded Diovan and Exforge product did not contain nitrosamines. (ECF 2023-10, Health Canada at 10). Moreover, for context, even if this were a reasonably disputed issue it would be an issue on the merits, not class certification.

This argument is an extension of Defendants' apparent strategy to try to prove that the branded drugs contained nitrosamines and thus no harm, no foul, despite that nitrosamines were not approved to be in those drugs and were never found to be in those drugs by Defendants or the regulatory authorities. Further, Defendants' own experts opine that the compendial requirements for Diovan and Exforge, such as the USP Monographs, set the characteristics and specifications required for a drug to hold a USP grade designation. (ECF 2023-7, Clevenger Dep. Tr. 66:14-67:17; ECF 2036-3, Sheinin Expert Rpt. at ¶ 38-40; Williams Dep. Tr. 126:12-127:13, Ex. B). The USP establishes nitrosamines to be unacceptable impurities in VCDs. (ECF 2023-6, USP Nitrosamine Impurities Webpage).

Defendants inaccurately cite to Dr. Najafi's deposition to support their contention that Dr. Najafi improperly assumed that the RLDs do not contain NDMA or NDEA. (Def. Br. at 5; Najafi Dep. Tr. 139:24-140:7). But a review of relevant excerpts from Dr. Najafi's deposition transcript reveals that the Defendants cut Dr. Najafi off when he began to explain that he wasn't making an

assumption, but instead had utilized the underlying chemistry at play in the various manufacturing processes – and also clarified that he had not presented his full merits opinions at this stage:

> [Mr. Trischler] [redacted]

(ECF 2033-4, Najafi Dep. Tr. 138:17-140:7 (emphasis added)). Defense counsel refused to accept Health Canada's testing as an adequate basis for Dr. Najafi to rely on and did not allow Dr. Najafi to get into how the chemistry underlying the manufacturing process also supports his opinion that with proper cGMP the RLD manufacturing process would not create nitrosamines. Of course, this

has been recognized by the Defendants themselves, for example ZHP'S Deviation Investigation Report, which sets forth the aspects of its [redacted]. (PRINSTON00075797 at 810-811, 818-819, Ex. C). Instead of asking questions rooted in the facts, defense counsel continued to shoehorn the word assumption in his questions and repeatedly characterized the basis of Dr. Najafi's opinion as an assumption, merely because defense counsel thought there might be alternative evidence out there somewhere showing some level of NDMA in the RLD.[2] The record, however, is clear. Dr. Najafi relied on Health Canada's testing data (as was disclosed in his materials considered) and his personal knowledge on the chemistry underlying nitrosamine formation. (Najafi Dep. Tr. 219:12-222:21), and the FDA has never suggested that there were nitrosamines in the RLD. This is far from a "baseless assumption." Most important, the methodology used to identify these foundational facts for the class opinions is reliable.

D. NDMA and NDEA are Unacceptable Impurities in VCDs

Defendants also argue that generic and branded drugs can have different levels of impurities, and that by opining NDMA and NDEA are unacceptable impurities in VCDs, "Dr. Najafi has conjured a regulatory standard that no agency applies." (Def. Br. at 7). They partially cite to Dr. Najafi testifying that "[t]he FDA does not require [] the generic drug manufacturer to match every impurity of the branded drug." (Najafi Dep. Tr. 19:13-15). This much is true, but it does not render

[2] Even if a RLD tested positive for the presence of NDMA or NDEA, it would be irrelevant. What is relevant is that the RLDs have tested negative for the presence of NDMA and NDEA, further verifying that with proper cGMP VCDs can be manufactured without any NDMA or NDEA. Therefore, if an RLD tests positive for the presence of NDMA or NDEA, it merely indicates that the name brand manufacturer had cGMP deficiencies with regard to a particular batch – which has never been found by any regulatory authority.

Dr. Najafi's opinion unreliable. For one, not all impurities are the same. An innocuous impurity in a generic drug might not breach a duty of sameness. But a *dangerous genotoxic* impurity, such as NDMA or NDEA, beaches the duty of sameness. We know this since that is the reason for the recall – a fact the Defendants continually ignore. As Dr. Najafi's full answer that Defendants only partially quote reads:

> [Mr. Trischler] [redacted]
>
> [redacted]

(ECF 2033-4, Najafi Dep. Tr. 19:9-15 (emphasis added)). NDMA and NDEA are not safe impurities. Dr. Najafi cites to the 2015 and 2018 versions of M7(R1), a guidance to the pharmaceutical industry published by the FDA that lists NDMA and NDEA among a small handful of high potency DNA reactive mutagens referred to as the *cohort of concern* to support that NDMA and NDEA are not safe impurities. (Najafi Expert Declaration at ¶ 27). This group of impurities is excepted from the TTC (Threshold of Toxicological Concern) approach of establishing baseline acceptable levels, and are instead subjected to specific analysis as occurred here leading to the 96 ng level established for NDMA and 26.5 ng level for NDEA, by the FDA. The *cohort of concern* impurities are believed to have negative health effects *regardless of the amount present* in the drug and are therefore considered unacceptable impurities and are more stringently controlled. (ICH M7(R1) 2015 at 8, Ex. D; ICH M7(R1) 2018, ECF 1711-6 at 7).

Regulatory agencies consider NDMA and NDEA to be dangerous impurities in VCDs, regardless of the amount present. Therefore, Dr. Najafi did not "conjure a regulatory standard that no agency applies" by opining that NDMA and NDEA are unacceptable impurities in VCDs.

III. Dr. Najafi May Opine on the Carcinogenicity of NDMA and NDEA

Defendants argue that Dr. Najafi is "profoundly unqualified to offer any opinion regarding the carcinogenicity of NDMA or NDEA." (Def. Br. at 17). However, Dr. Najafi is permitted to rely on regulatory determinations, as he does as an organic chemist, that NDMA and NDEA are highly potent DNA reactive mutagens that fall within the *cohort of concern*, to support his opinion that the presence of NDMA or NDEA in Defendants' VCDs renders their VCDs to not be the "same as" or "chemically equivalent to" or "generic equivalent to" the brand name Diovan or Exforge products. Dr. Najafi is not offering a causation opinion by stating that "NDMA and NDEA are carcinogenic and should not be present in any drug." (Najafi Expert Decl. at ¶ 30). Rather, Dr. Najafi is distinguishing between acceptable impurity differences and unacceptable impurity differences a drug can have from the RLD. Dr. Najafi testified repeatedly during his deposition that the hazardous nature of the impurity is what makes the difference, and as the Court can see from the excerpt below, defense counsel simply refused to hear the answer and instead of moving on he resorted to threatening Dr. Najafi:

[Mr. Trischler] [redacted]

[redacted]

*****

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

*****

[redacted]

(Najafi Dep. Tr. 12:7-15, 14:10- 15:20, 16:22-18:3 (emphasis added) (objections omitted)).

The reason that NDMA and NDEA are not treated like benign impurities, or even like most harmful impurities, is because they are genotoxic "cohort of concern" impurities, and extremely carcinogenic. In coming to his opinion that NDMA and NDEA are unacceptable impurities that render them not the same as the RLD, Dr. Najafi appropriately relied on FDA guidance statements, such as ICH M7(R1), which notes:

> Some structural groups were identified to be of such high potency that intakes even below the [Threshold of Toxicological Concern] TTC would theoretically be associated with a potential for a significant carcinogenic risk. This group of high

> potency mutagenic carcinogens, referred to as the *cohort of concern*, comprises aflatoxin-like, N-nitroso-, and alkyl-azoxy compounds.

Most defense experts, such as Dr. Williams, rely on the exact same regulatory document:

(Williams Dep. Tr 78:14-79:12, Ex. B (emphasis added)).

Dr. Najafi can also rely on ICH M7(R1), which defines N-nitroso compounds as highly potent mutagenic carcinogens that need be controlled based on their potency to an amount "at or below the acceptable cancer risk level", to opine that because NDMA and NDEA are highly potent mutagenic carcinogens their presence in Defendants' VCDs rendered them not the same as the RLDs. (ICH M7(R1) 2015 at 8, Ex. D).

IV. Defendants' Various Arguments About Other "Facts" Is Irrelevant to the Admissibility of Dr. Najafi's Opinions

Defendants variously argue that Dr. Najafi's conclusions must be wrong based on a series of factual arguments intended to muddy the water on a class certification opinion, including (i) some of them conducted their own testing and did not find nitrosamines in their VCDs, (ii) the levels of

nitrosamines in Defendants' VCDs varied, and (iii) third-party testing of product of unknown origin or provenance may have found nitrosamines in a non-US, outsourced version of Diovan. All of these arguments are misguided. None of them go to the admissibility of Dr. Najafi's class certification opinions. Rather, disputes over other facts and their import are classic matters of weight and credibility. *See, e.g.*, *In re Johnson & Johnson Talcum Powder Prod. Mktg., Sales Pracs. & Prod. Litig*., 509 F. Supp. 3d 116, 184 (D.N.J. 2020) ("the fact that experts may disagree as to how to interpret the relevant studies at issue does not indicate one expert is more reliable than the other. Moreover, to the extent there are competing studies relied upon by the parties' experts, a weighing of those studies is reserved for the factfinder at trial."); *In re TMI Litig. Cases Consol. II*, 922 F. Supp. 1038, 1043-44 (M.D. Pa. 1996) ("the failure to consider certain potentially relevant data goes to the weight of the testimony").

A. Testing Conducted by Regulatory Agencies is Reliable and Testing Conducted by Defendants on Their Own Product While in Litigation May Be Inherently Unreliable

1. Results From a Regulatory Agency Do Not Need to be Validated by a 3rd Party

Defendants downplay testing conducted by regulatory agencies, because Dr. Najafi's "lab never validated" the results of the very regulatory agencies that developed and published the validated methods to detect nitrosamines in VCDs.[3] (Def. Br. at 13). Dr. Najafi does not need to validate the testing conducted by a regulatory agency to rely on them, and Defendants do not cite to any authority to support the notion that he needs to. Dr. Najafi and other experts in his field reasonably rely on testing conducted by regulatory agencies in forming their opinions, which is all that FRE 703 requires.

[3] Defendants are seemingly conceding that Dr. Najafi is a highly competent chemist and that his laboratory generates such reliable results that if Dr. Najafi's results were different than a regulatory agency's, the regulatory agency's results would be invalid, not Dr. Najafi's.

2. Aurobindo's Internal Testing is Unreliable

While downplaying the testing results from regulatory agencies, Defendants also play up testing conducted by an interested party in this litigation—Aurobindo—to argue that a "core assumption" underlying Dr. Najafi's opinion is "demonstrably false"—that VCDs contained NDMA or NDEA. (Def. Br. at 5). Plaintiffs previously laid out in great detail why Defendant Aurobindo's internal testing[4] results are unreliable, in part because Aurobindo was repeatedly unable to detect any NDEA in the exact same batches in which the FDA repeatedly detected NDEA above the allowable limits. (Plfs. Br. Preclude Clevenger at 8-9, ECF 2047-1; APL-MDL-2875-0102832 at 835, 859-861, ECF 2047-6). Even the regulatory consultant that Aurobindo hired for non-litigation purposes concluded that "[t]he Aurobindo testing method [redacted]" and that "[i]n-house results are [redacted]." (APL-MDL-2875-0135474, ECF 2047-7). Furthermore, Aurobindo itself previously conceded in its Aberrant Result Investigation Report that [redacted] could have been due to [redacted]." (APL-MDL-2875-0076155 at 173, ECF 2047-8). Aurobindo's conclusion that the [redacted] isn't surprising, considering that instead of testing VCDs in marketable packs, Aurobindo just put its VCDs in a [redacted].[5] (APL-MDL-2875-0076155 at 173, ECF 2047-8).

Defendants claim that not all Defendants' VCDs contained NDMA or NDEA, as evidenced by Aurobindo not recalling all of its valsartan, because Aurobindo's internal testing did not detect

[4] Aurobindo utilized a testing methodology [redacted]." (Clevenger Dep. Tr. at 119:1-4; APL-MDL-2875-1296768 at 71-72, Ex. E).

[5] [redacted] (APL-MDL-2875-0076155 at 173, ECF 2047-8).

any NDMA or NDEA.[6] (Def. Br. at 5). Defendants are correct that Aurobindo did not detect any NDMA or NDEA in some batches of its VCDs, but that doesn't mean those VCDs didn't contain NDMA or NDEA. Defendants only cite to Aurobindo's initial December 31, 2018, recall of 80 lots of VCDs to support that Aurobindo only recalled certain batches. Aurobindo's new legal counsel must have been unaware of the opinion that Aurobindo's regulatory consultant came to after learning that Aurobindo wasn't detecting NDEA in the same batches of VCDs that the FDA repeatedly detected NDEA at levels above the allowable limit—that is, "[redacted]." (APL-MDL-2875-0048766 at 768, ECF 2047-5). Aurobindo's new legal counsel must have also been unaware that just as Aurobindo's regulatory consultant predicted, additional lots[7] of Aurobindo's VCDs were recalled "due to unacceptable amounts of N-Nitrosodiethylamine (NDEA) found in the medicine." (APL-MDL-2875-0687069, Ex. F). Aurobindo then ceased selling VCDs in the United States and their DMF went inactive because it was determined that manufacturing VCDs via the toluene route was **not safe**. (4/30/2021 Dr. Rao Dep. Tr. at 225:19-228:6, Ex. G).

Based on testing methods that Aurobindo knew were producing artificially low results that were inconsistent with the testing results of a regulatory agency, Aurobindo continued to release VCDs containing unsafe levels of nitrosamines into the US market for over half a year after other Defendants had recalled all of their VCDs. Defendants' focus here simply spotlights a punitive damages issue—Aurobindo's decision to continue selling contaminated VCDs based on knowingly

[6] The FDA detected either NDMA or NDEA in every single lot of Aurobindo VCDs tested. (Auro-MDL-2875-0105928, Ex. H).

[7] The FDA's website and an [redacted] both note an additional 38 lots of Aurobindo VCDs were being recalled on March 1, 2019, while the recall letter produced by Aurobindo only notes [redacted] lots. (*Cf.* https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-angiotensin-ii-receptor-blocker-arb-recalls-valsartan-losartan, Ex. I and APL-MDL-2875-0687069, Ex. F with Auro-MDL-2875-0081255, Ex. J).

inaccurate testing results—undermining any claim that Aurobindo acted as a responsible company. However, this in no way undermines Dr. Najafi's opinions, nor does it support Defendants' claim that Dr. Najafi relied on a "demonstrably false" assumption.

3. Teva's Internal Documents Undermine the Relevance of the Teva VCDs in which the FDA Did Not Detect NDMA/NDEA and Draw Into Question What VCDs Teva Actually Shipped to the FDA for Testing

Defendants claim that "Dr. Najafi's core assumptions are incorrect"—that Defendants' VCDs contained NDMA or NDEA, and that the RLDs should not contain NDMA or NDEA—and then cite to the FDA's public VCD testing results (FDA VCD Lab Analysis, ECF 2033-7) as evidence that "certain lots of amlodipine valsartan manufactured by Teva using Mylan's API and tested by FDA did not contain detectable levels of NDMA or NDEA." (Def. Br. at 5). A December 6, 2018, email from the FDA to Teva reveals that only two batches or lots of Teva's amlodipine valsartan had no detectable levels of NDMA or NDEA. (TEVA-MDL2875-00686472, Ex. K). The two Teva VCD batches that the FDA did not detect NDMA or NDEA in were 26X055 and 22X047. (Ex. K). Plaintiffs do not dispute the reliability of the FDA's testing results but do question what Teva actually sent to the FDA for testing and the relevance of what the FDA tested.[8]

a. Teva Batch 26X055 Never Entered the Stream of Commerce and was Out of Specification for Other Impurities

Within an NDA/ANDA field alert submitted by Teva on December 9, 2019 to the FDA, Teva disclosed that VCD batch 26X055 and several other batches[9] "were not released to commerce and have been quarantined." (TEVA-MDL2875-00166763 at pg. 5, Ex. L). It is irrelevant if batch

[8] Teva was experiencing systemic deficiencies in its quality management system as evidenced by selling VCDs for years containing genotoxic carcinogens. As such, all VCD related data generated by Teva and its defunct quality management system should receive increased scrutiny.

[9] Teva also sent the FDA lots 26X053 and 26X054 to test, which were again lots that never entered the stream of commerce and were some of the least contaminated Teva VCDs tested. (Ex. L; FDA VCD Lab Analysis, ECF 2033-7).

26X055 actually had non-detectable levels of NDMA and NDEA, because the batch never entered the stream of commerce and therefore no Plaintiff bought or consumed VCDs from batch 26X055.

Batch 26X055 was manufactured in July of 2017 and tested [redacted] (greater than 0.1% impurity level). (TEVA-MDL2875-00307398, Ex. M; TEVA-MDL2875-00475626 at row 6176 column G, Ex. N[10]). Defendants' experts agree that no individual impurity can exceed 0.1%. (ECF 2023-7, Clevenger Dep. Tr. 67:21-25; ECF 2036-2, Sheinin Dep. Tr. 110:20-111:12; ECF 2044-1, Lambert Expert Rpt. at ¶ 81; Baertschi Expert Rpt. at ¶ 31, Ex. O). It is irrelevant that Teva batch 26X055 did not have detectable levels of NDMA or NDEA, because batch 26X055 was already not the generic equivalent of the RLD due to exceeding the allowable level of valsartan Impurity D.

Batch 26X055 contained [redacted]. (Ex. N at row 6176 columns W, AA). Defendants confirmed in 2018 that they had [redacted] of lot 26X055 currently in their inventory. (TEVA-MDL2875-00025620 at 21, Ex. P). Defendants sent all [redacted] from lot 26X055 to be destroyed. (TEVA-MDL2875-00095898 at 901, Ex. Q). It is quite perplexing how Teva could have destroyed all [redacted] units of batch 26X055 and still sent the FDA VCDs from batch 26X055 to test.[11]

Assuming that the VCDs Teva sent to the FDA were actually from batch 26X055, what will eventually be relevant is why exactly Teva decided to send VCDs to the FDA for testing[12] that

[10] A digital version of this spreadsheet will be emailed to the Court since the PDF version of the spreadsheet cuts off relevant information and is difficult to match up the data to the associated lot.
[11] Likewise, Teva both packaged and destroyed [redacted] units of batch 26X054, yet Defendants claim they also sent VCDs from batch 26X054 to the FDA to test. (Ex. N at row 6175 columns W, AA; Ex. Q at 900).
[12] Of note, Teva refused to send the FDA samples of its VCDs until Teva had tested the VCDs and knew what the results would be of the VCDs before deciding which VCDs to send the FDA. Teva even requested that the FDA accept a letter stating it was not possible for NDMA to be in their VCDs in lieu of the FDA testing their VCDs. (TEVA-MDL2875-00004495, Ex. R).

never entered the stream of commerce and never should have even been under consideration for sending into the stream of commerce, because Teva's own testing concluded that the batches[13] were out of specification due to the presence of [redacted]. (TEVA-MDL2875-00168156, Ex. S; Ex. M).

b. Teva Batches 26X055 & 22X047 were Manufactured with Adulterated API

Concerningly, Teva was able to easily identify what API lots were utilized in all the batches of VCDs, except for the two batches (26X055 & 22X047) that the FDA was unable to detect NDMA or NDEA in. (Ex. K). Even more troubling, the API lots that Teva eventually claimed were used in batches 26X055 and 22X047 all tested positive for either NDMA or NDEA.

Teva claims that batch 26X055 utilized Mylan API lots [redacted]. (Ex. K). Mylan API lot [redacted]ing. (MYLAN-MDL2875-00264679 at 81, Ex. T). Mylan API lot [redacted]. (Ex. T at 81). Furthermore, batch [redacted], but the FDA detected above allowable limits for NDMA in batch 26X054. (Ex. K). It defies logic that batch 26X055 had no detectable level of nitrosamines present when batch 26X055 was manufactured with nitrosamine adulterated APIs, and the other VCDs that were manufactured with the exact same nitrosamine adulterated APIs tested above the allow limits for nitrosamines. The anomalous results for batch 26X055 further support the notion that the VCDs Teva sent the FDA weren't actually from batch 26X055.

Teva claims that batch 22X047 utilized Mylan API lots [redacted]. (Ex. K). Mylan API lot [redacted] (Ex. T at 81). Mylan API lot [redacted]. (Ex. T at 81). Mylan API lot [redacted]

[13] Batches 26X054 and 26X053 also exceeded the allowable limit of [redacted]. (Ex. M; FDA VCD Lab Analysis, ECF 2033-7).

testing. (Ex. T at 81). Like batch 22X047, batch 22X046 only used Mylan API lots [redacted], but the FDA detected above the allowable limits of NDMA in batch 22X046. (Ex. K). Furthermore, batch 22X045 also utilized Mylan API lots [redacted] and the FDA detected above the allowable limits of NDEA in batch 22X045. (Ex. K). It is again illogical that batch 22X047 actually had no detectable level of nitrosamines present when batch 22X047 was manufactured with nitrosamine adulterated APIs, and other batches manufactured with the exact same nitrosamine adulterated APIs tested above the allowable limits for nitrosamines. The anomalous results for batch 22X047 draw into question whether the VCDs that Teva sent to the FDA were actually from batch 22X047.

While it is unclear if Teva actually sent the FDA VCDs from batches 22X047 or 26X055, it is clear that both batches were manufactured exclusively with API adulterated with genotoxic carcinogens. The fact that Teva utilized APIs adulterated with NDMA and NDEA to manufacture their VCDs only adds support to Dr. Najafi's opinion—Defendants' VCDs contained NDMA or NDEA. Regardless, the manufactured issue of whether the Defendants' VCDs contained NDMA or NDEA—despite the recall and the mass of documents showing they were—is a question of fact at this point.

B. A Third Party (Valisure) Detecting 17ng of NDMA in Novartis Valsartan is Irrelevant

1. The RLD Holder Experiencing a Deficiency in Their Quality Management System Would Not Relieve Defendants from Their Current Liability Resulting from Their Own Deficient Quality Management Systems

Defendants ignore that Dr. Najafi relied on the testing results of Health Canada and his own knowledge on the chemical process utilized to create the RLD in offering his opinion that the RLD should not contain NDMA or NDEA, and Defendants again incorrectly profess that Dr. Najafi's opinion is "based on assumptions that are not supported by the facts in record." (Def. Br. at 12). Defendants appear to be putting forth an argument that if any non-regulatory or non-governmental

third party ever publishes testing results showing any amount of NDMA or NDEA in Novartis's RLD products, then the Defendants liability in this litigation magically disappears. (Def Br. at 13-16). It is important to note that despite Valisure submitting these results to the FDA in 2019, the FDA has never adopted those results or confirmed that the branded drug contained nitrosamines.

However, it would be irrelevant even if one were to detect NDMA or NDEA in Novartis's RLD. What is relevant is that regulatory testing has confirmed that Novartis's RLD can be manufactured without any detectable amount of NDMA or NDEA. (Health Canada at 10, ECF 2023-10). If NDMA or NDEA is ever legitimately detected in Novartis's RLD[14], it would only indicate that Novartis was failing to meet cGMPs by manufacturing nitrosamine adulterated VCDs at some point. A cGMP deficiency by the name brand manufacturer would in no way alleviate or even lessen Defendants' liability for their own cGMP deficiencies.

2. There is No Evidence that Dr. Najafi or his Laboratory Ever Detected NDMA in Novartis's RLDs

Defendants claim that Dr. Najafi and his laboratory eviscerated the foundation of his opinion by finding evidence of NDMA in the RLDs. (Def. Br. at 13). This argument is simply a rehash of Defendants' motion to compel Dr. Najafi's confidential testing results. (ECF 2013-1). Furthermore, Dr. Najafi has reviewed his testing data and has explained that the testing he performed does not support the notion that Novartis's RLD contained NDMA. (Najafi Declaration, ECF 2023-3).

3. Defendants Make Unsupported Assumptions to Argue that the Third Party Valisure Tested Novartis's RLD and Not Novartis's Generic VCDs

Without knowing how Valisure obtained the VCD samples it tested, Defendants claim the samples must have been name brand product intended for the United States, simply because

14 [redacted] (*See* ECF 2023 at 5-6).

Valisure requested the FDA to recall certain VCDs in the United States. (Def. Br at 14). [redacted]. (Def. Br. at 14 (emphasis added)). But, unlike the Health Canada testing results which specifically indicate that they tested Novartis Diovan, Valisure only notes that it tested Novartis valsartan (the generic name of Diovan is valsartan). (*Cf*. Health Canada at 10 , ECF 2023-10 with Valisure Citizen Petition at 7, ECF 1984-1). This is a different drug manufactured with a different process.

4. Defendants Concede It's Not Surprising that Sourcing API from Multiple Vendors Will Result in Different Impurity Profiles

Numerous Defendants have repeatedly advanced the weak excuse throughout this litigation that there was no way for them to anticipate the nitrosamine impurities when they were changing their sourcing vendors and manufacturing processes. When it comes to Novartis, however, Defendants candidly admit that "[redacted]." (Def. Br. at 14). Defendants are right that it's not surprising that sourcing API from multiple vendors utilizing different manufacturing processes would likely result in different impurity profiles. This is why Defendants should have implemented cGMP compliant processes to identify the potential for impurities such as NDMA and NDEA to be created and to test to ensure they were not in their VCDs. However, we know that a European Novartis entity eventually identified the NDMA in ZHP's valsartan API because it was sourcing API from multiple vendors to manufacture generic valsartan manufactured with the cheaper generic processes.

Ultimately, the focus on the Valisure petition is a red herring, as this is an entity that Plaintiffs are not using in this litigation for any purpose, and nor does Dr. Najafi have access to internal Valisure documents or processes. As stated above, even if Defendants' constructed reality

were accurate, it would be irrelevant because all that matters is that RLDs are not supposed to have nitrosamines—part of the mutagenic *cohort of concern*—in them, and their generic equivalents should not contain nitrosamines either. The presence or absence of nitrosamines in any VCD does not impact the foundational validity of Dr. Najafi's opinion that VCDs should not contain NDMA or NDEA, and that VCDs that do contain NDMA or NDEA are not the same as, or chemical equivalent to the RLDs. As to the underlying fact questions Defendants focus on trying to create, the law of this Circuit is clear that such attacks go to weight, not admissibility. *See, e.g.*, *In re Johnson & Johnson Talcum Powder Prods. Mktg., Sales Pracs. & Prods. Litig.*, 509 F. Supp. 3d 116, 194-95 (D.N.J. 2020) (defense expert's "deliberate choice to not review [certain] articles identified by Plaintiffs [] does not render her opinion inadmissible").

CONCLUSION

For the foregoing reasons, Defendants' motion to exclude the class certification opinions of Dr. Ron Najafi—that VCDs containing NDMA an NDEA are not the same as the RLDs—should be denied. Dr. Najafi's core class certification opinion is that contaminated VCDs are a common issue for all class members. Dr. Najafi applied an appropriate methodology, relying on regulatory documents and testing information that one would be expected to consider in addressing this issue. Defendants' criticisms do not undercut the methodology behind the class certification opinions, and at most go to the weight, not the admissibility of Dr. Najafi's opinions.

Dated: June 2, 2022

Respectfully Submitted,

By: /s/ C. Brett Vaughn

C. Brett Vaughn RN, BSN, JD
Hollis Law Firm
8101 College Blvd, Suite 260
Overland Park, KS 66210
Phone: 913-385-5400
Fax: 913-385-5402
Email: Brett@HollisLawFirm.com

CERTIFICATE OF SERVICE

I hereby certify that on this 2nd day of June 2022, I caused a true and correct copy of the foregoing to be filed and served upon all counsel of record by operation of the Court's CM/ECF system. In addition, I certify that unredacted versions of the foregoing will be served contemporaneously upon liaison counsel for Defendants as well as the Court.

/s/ C. Brett Vaughn
C. Brett Vaughn